Introduction to the EPA Lead Models: Basics of Using the Integrated Exposure Uptake Biokinetic Model (IEUBK) and the Adult Lead Methodology (ALM)

Lead Modeling Training
ATSDR
July 24–25, 2007

Kevin Koporec, US EPA
Scott Sudweeks, US EPA
Aaron Yeow, US EPA
Mark Follansbee, SRC

Overview of Lead Model Training

- Introduction (why do we need models?)
- The IEUBK Model– structure and components
- The U.S. EPA Adult Lead Methodology (ALM)
- Discuss IEUBK & ALM inputs (review data entry windows and input variables)
- Risk Assessment Issues and Guidance
- PbB calculation, risk calculation, & PRG Examples

Lead Risk Assessment is Different

- A tremendous amount of information on the health effects of lead has been obtained through decades of medical observation and scientific research. By comparison to most other environmental toxicants, the degree of uncertainty about the health effects of lead is quite low.
- Some of these effects, particularly changes in the levels of certain blood enzymes and in aspects of children's neurobehavioral development, may occur at blood lead levels so low as to be essentially without a threshold.
- Therefore, EPA decided that it was inappropriate to derive a Reference Dose (RfD) for lead.
- EPA regulates lead exposure by using a biomarker (blood lead concentration).
- Environmental exposures to lead are modeled to predict blood lead levels associated with those exposures.
- In the early 90s, CDC established 10 µg/dL as the Federal level of concern (CDC 1991 is key citation).
- This differs from standard approach where RfD are used to derive hazard quotients.

OSWER Lead Risk Assessment Policy

- 1994 & 1998 OSWER Directives
  - Established the use of the IEUBK Model as the primary tool to generate residential risk-based soil cleanup levels.
  - OSWER's risk reduction policy is for no child to have greater than a 5% probability of having a blood lead level >10 µg/dL
  - OSWER's policy is that blood lead studies not be performed to attempt to calculate a site-specific GSD nor to attempt to "validate" the model. EPA generally recommends that if a blood lead study were to be performed, it should be performed for medical intervention purposes only and not for establishing long-term remedial or non-time-critical removal cleanup levels at sites.

- NAS (2005) concluded: "*Multicompartment predictive blood lead models are powerful tools for pediatric lead exposure risk assessments, for exploring lead risk management options, and for crafting remediation strategies. Their application to Superfund sites with environmental lead contamination is an important part of the CERCLA regulatory process.*"

Purpose of the Lead Models

IEUBK (Integrated Exposure Uptake Biokinetic Model)

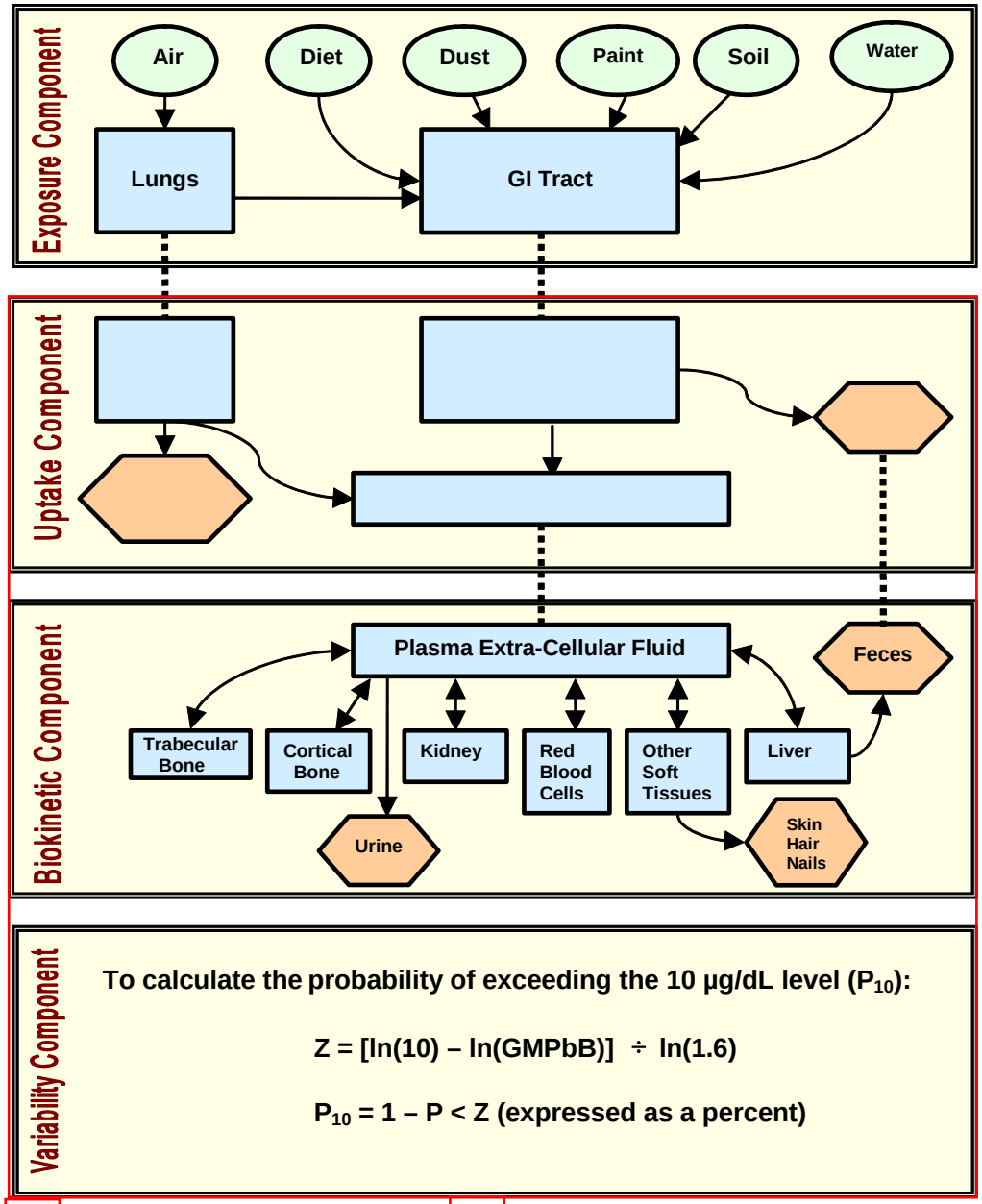
- Predicts the blood lead levels in children (under 7 years old) who are exposed to environmental lead from many sources
- Predicts the risk (probability) that a typical or hypothetical child exposed to specified media lead concentrations will have a blood lead level ≥10 µg/dL (the blood lead level of concern)
- Predicts PRG (cleanup levels) for various media in residential soil.

ALM (Adult Lead Methodology)

- Predicts the risk of elevated blood lead levels in non-residential settings (adult exposure to soil; ultimate receptor is fetus)
- Predicts PRG (cleanup levels) for soil in non-residential setting

Characteristics of the IEUBK Model

- While IEUBK model risk assessments are more complex than the typical Superfund risk assessment approach, the IEUBK model is not as complex as variance propagation approaches (PRA)
- The IEUBK model employs more site-specific information than other EPA risk assessment models
- The IEUBK model performs well when comparing predicted and observed blood lead levels (*Hogan et al., 1998. Integrated Exposure Uptake Biokinetic Model for Lead in Children: Empirical Comparisons with Epidemiologic Data. Environmental Health Perspectives, Vol. 106 No. S6*)


Exposure Component
Air
Diet
Dust
Paint
Soil
Water
Lungs
GI Tract
Uptake Component
Biokinetic Component
Plasma Extra-Cellular Fluid
Feces
Trabecular Bone
Cortical Bone
Kidney
Red Blood Cells
Other Soft Tissues
Liver
Urine
Skin Hair Nails
Variability Component
To calculate the probability of exceeding the 10 µg/dL level (P_{10}):
Z = [ln(10) – ln(GMPbB)] ÷ ln(1.6)
P_{10} = 1 – P < Z (expressed as a percent)
Environmental Media
Elimination Pools of the Body
Body Compartments
Body compartment or elimination pool required in more than one component

History of the IEUBK Model Development

IEUBK is the product of many years of development

1985-89: Office of Air Quality Planning Standards

1989: Development by Superfund following SAB review

1989-2001: DOS version (0.99d) development.

1994-2001: Release of 0.99d version by Superfund with input from EPA, ATSDR, CDC, and SAB.

1998: Independent Validation and Verification Conference

1997-2001: IEUBK (0.99d) was converted to Windows

2001-present: IEUBK 1.0 and refinement continue

Independent Reviews of the IEUBK

The reviewers have generally found that the model was scientifically sound and useful for lead risk assessment

1990 SAB review for NAAQS

1992 SAB review and External Peer Review of model

1998 Independent Validation and Verification

1998 SAB review for TSCA Section 403 Regulation

2005 National Academies of Science (NAS) review for Coeur d'Alene site report

IEUBK Exposure Module Components

Media Concentrations for Input		
Soil	Soil must be sampled. Site-specific data required.	Refer to the IEUBK User's Guide and 1994 Guidance Manual for additional information on this input parameter.
Dust	Site-specific data or a value can be derived from soil concentration using multiple source analysis.	Refer to the IEUBK User's Guide and 1994 Guidance Manual for additional information on this input parameter.
Air (default)	0.1 µg/m^3	Ratio of indoor to outdoor air lead concentration is 30%. Site-specific data may be substituted.
Drinking Water (default)	4 µg/L	Site-specific data may be substituted.

IEUBK Components (continued)

Media	Age-specific Intake Rates							Comments
	0-1 year	1-2 yrs	2-3 yrs	3-4 yrs	4-5 yrs	5-6 yrs	6-7 yrs	
Soil/dust (mg/day)	85	135	135	135	100	90	85	Default values recommended. Intake is apportioned 55% dust & 45% soil
Air (m^3/day)	2	3	5	5	5	5	7	Default values recommended
Drinking Water (L/day)	0.2	0.5	0.52	0.53	0.55	0.58	0.59	Default values recommended
Diet (µg Pb/day)	3.16	2.6	2.87	2.74	2.61	2.74	2.99	Site-specific data may be used to assess exposure to fish, game, or home-grown produce.
Alt. Source	Site-specific data may be used to account for intake of lead in other sources							Refer to the IEUBK User's Guide and 1994 Guidance Manual for more information

Intake – Uptake – Biokinetic Relationship

Daily **Intake** of lead is calculated as follows:

Intake = Media Concentration x Media Intake Rate

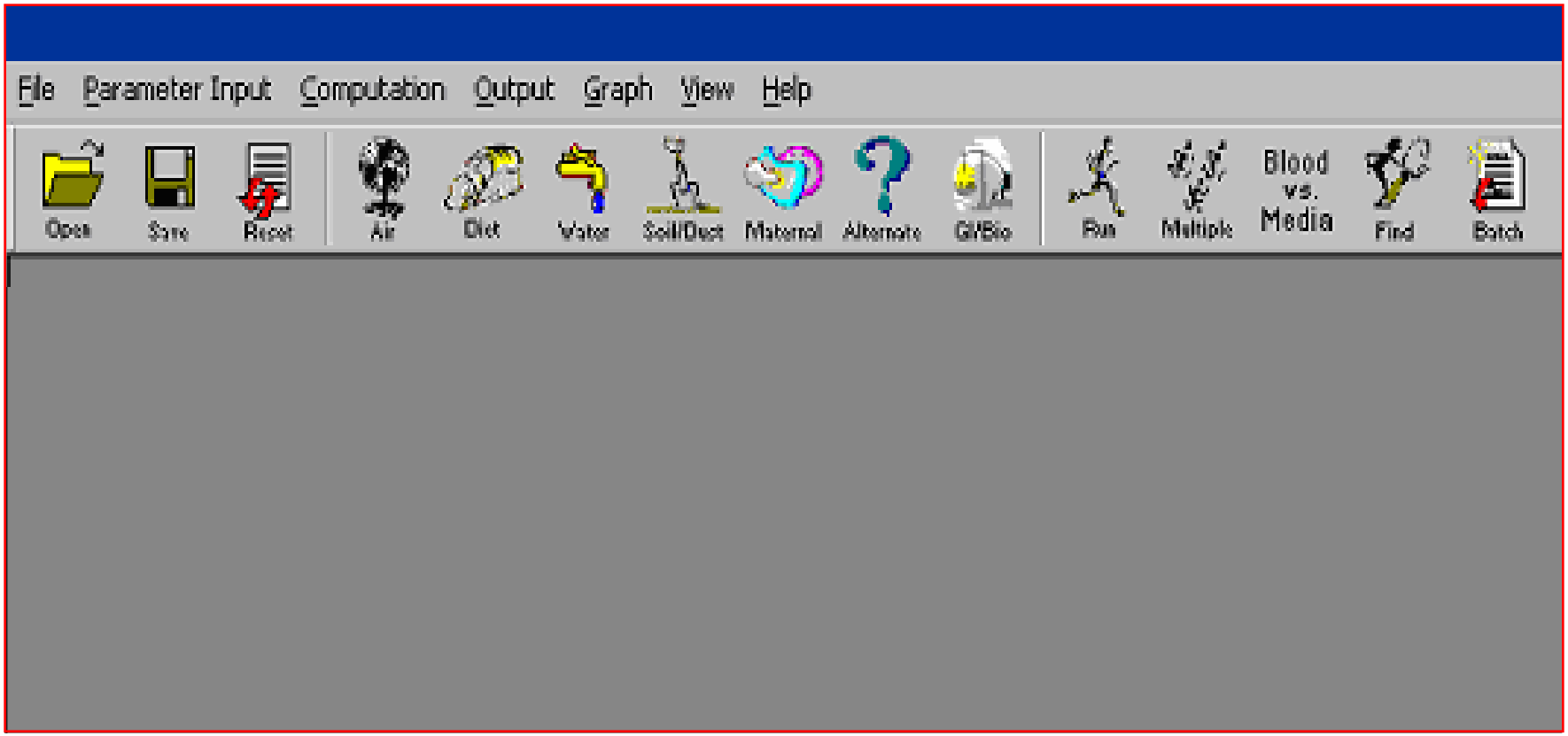
For example: µg lead/day = (µg lead / g of media) x (g of media / day)

Uptake is calculated based on media-specific absorption values (defaults are available): Uptake = Intake x Absorption Factor

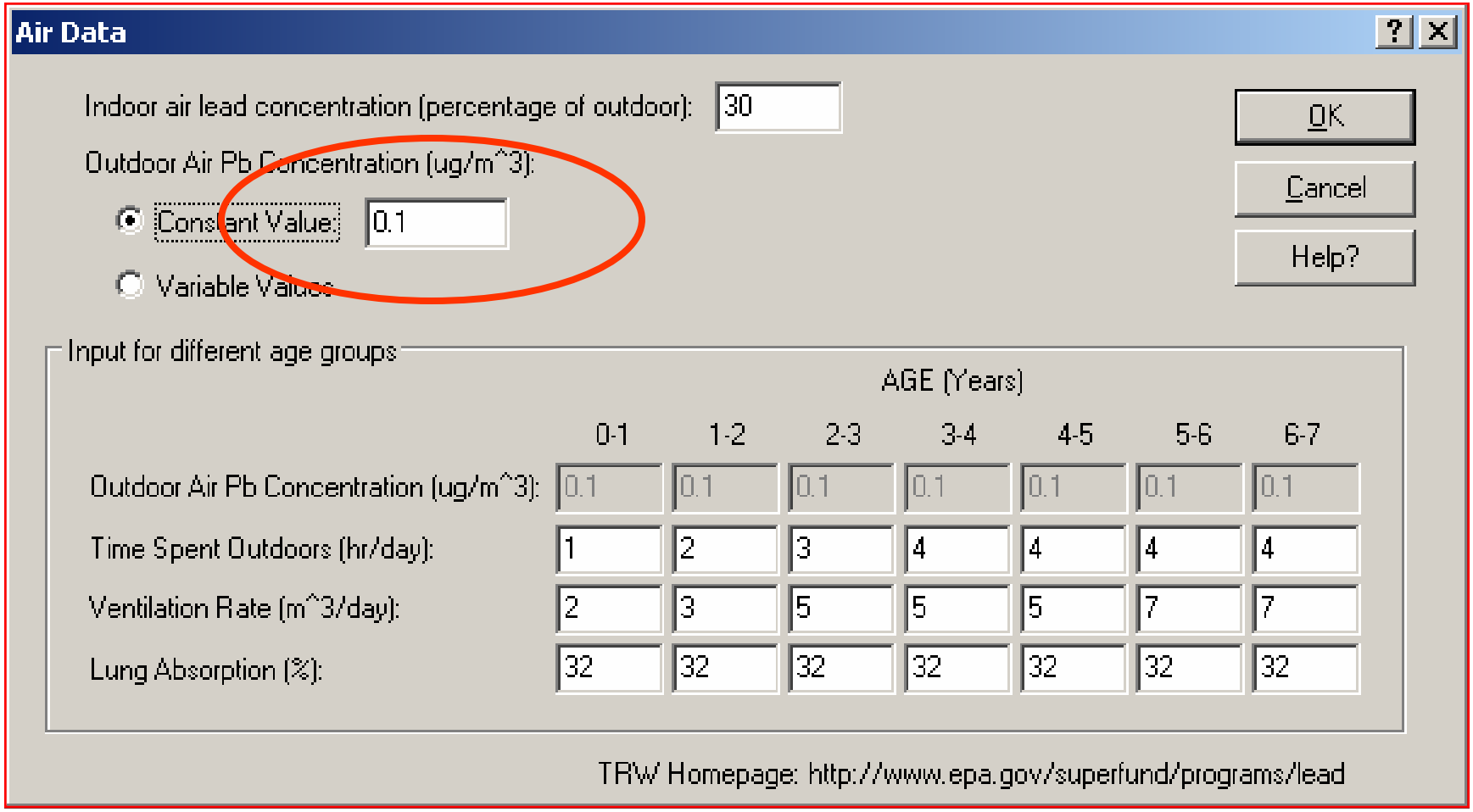
Biokinetic module estimates transfer rates for Pb moving between compartments and through elimination pathways to derive a predicted long-term steady state geometric mean PbB concentration.

In the final step, the **Probability** module estimates a plausible distribution of PbB concentrations for a given GSD. The distribution is centered on the geometric mean PbB concentration calculated by the Biokinetic Module.

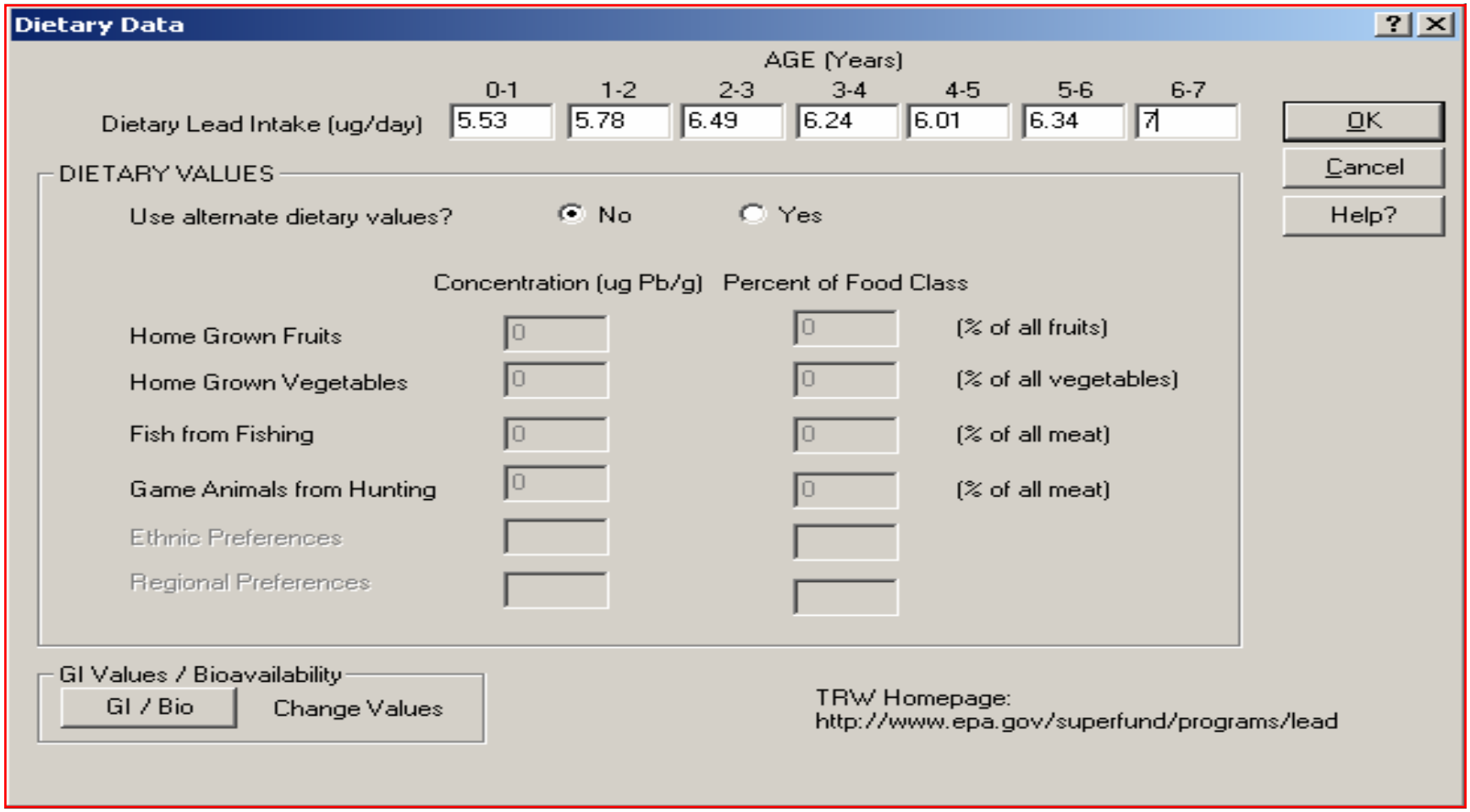
IEUBK Model Media Selection Window



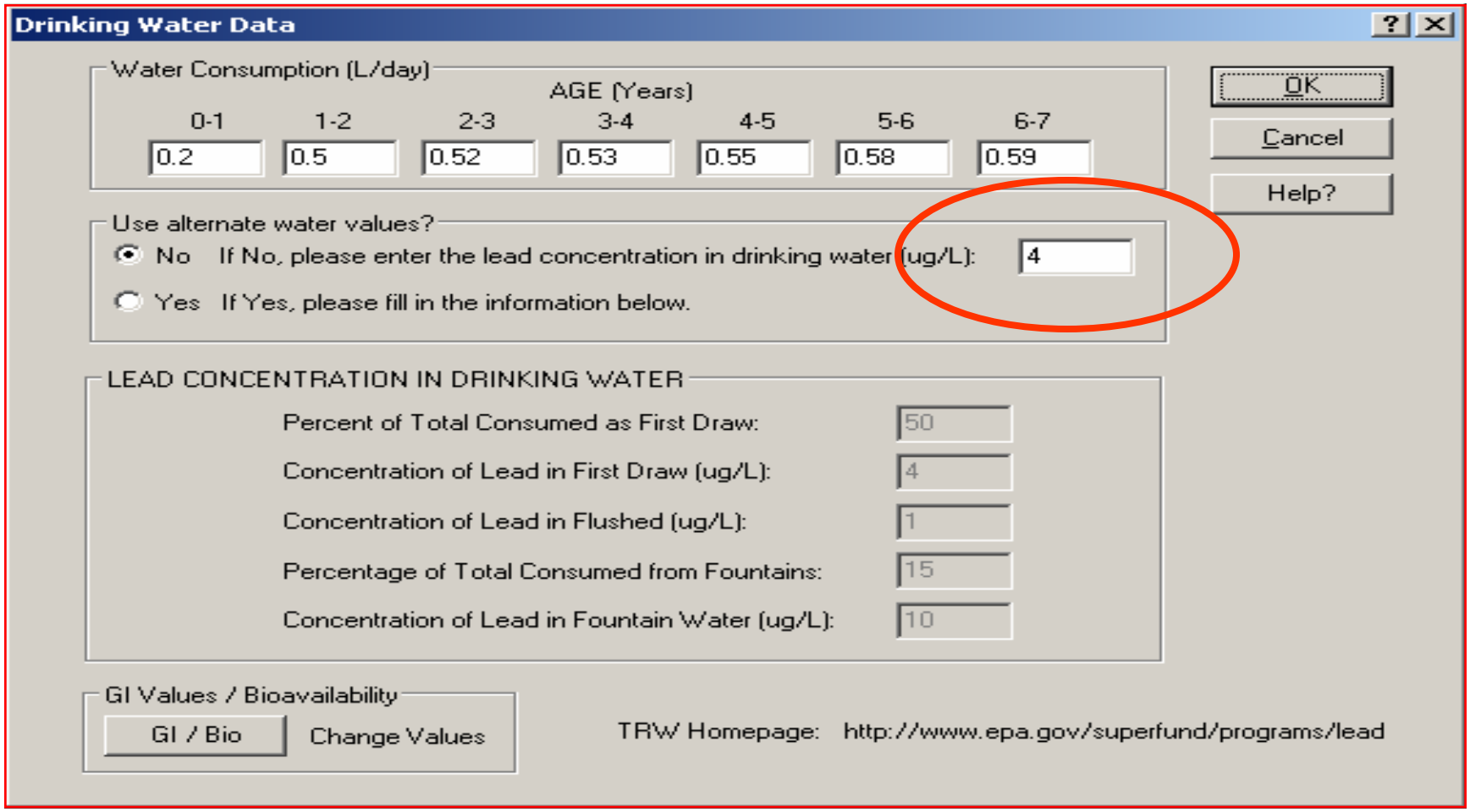
Air Exposure Input



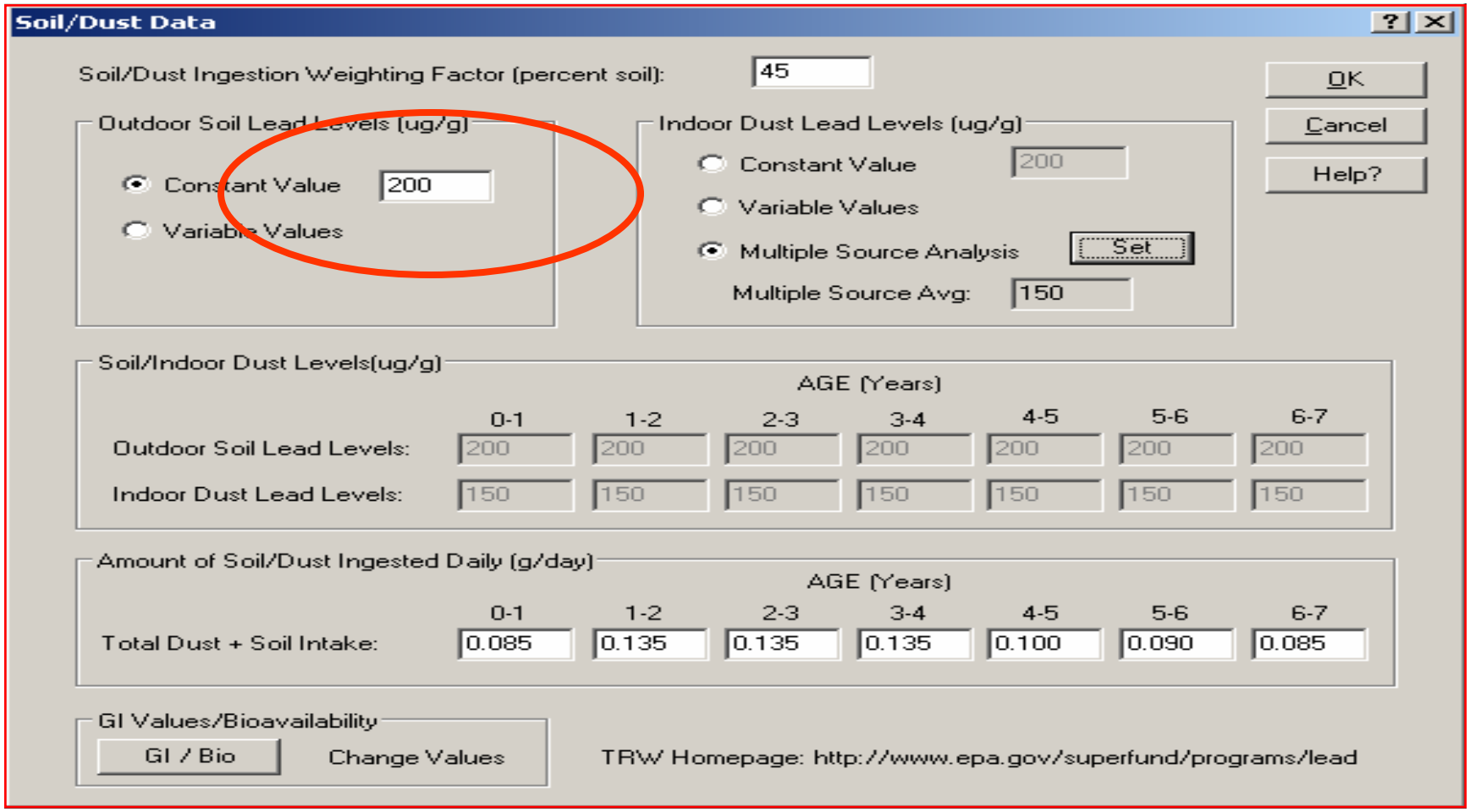
Dietary Exposure Input



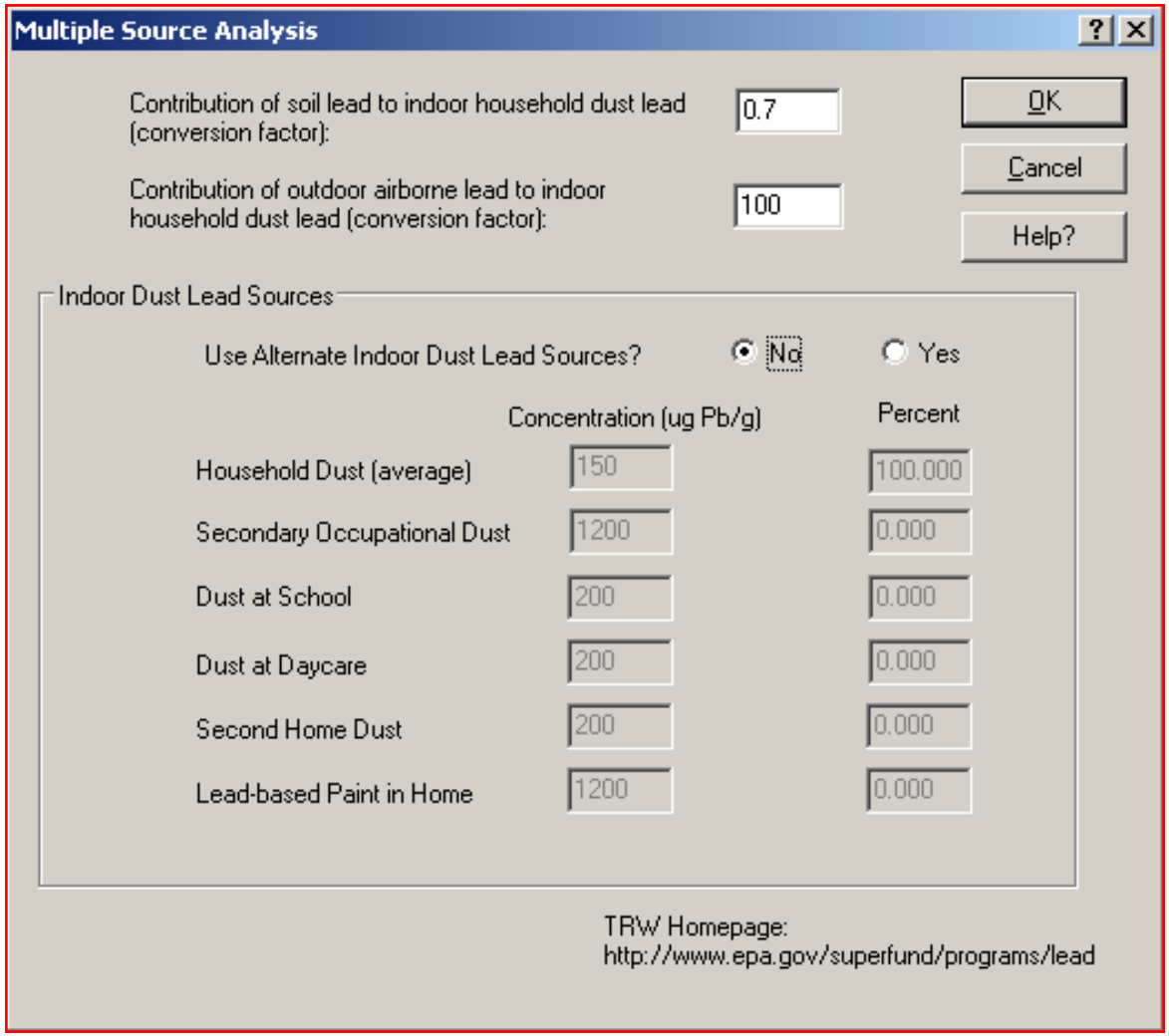
Drinking Water Exposure Input



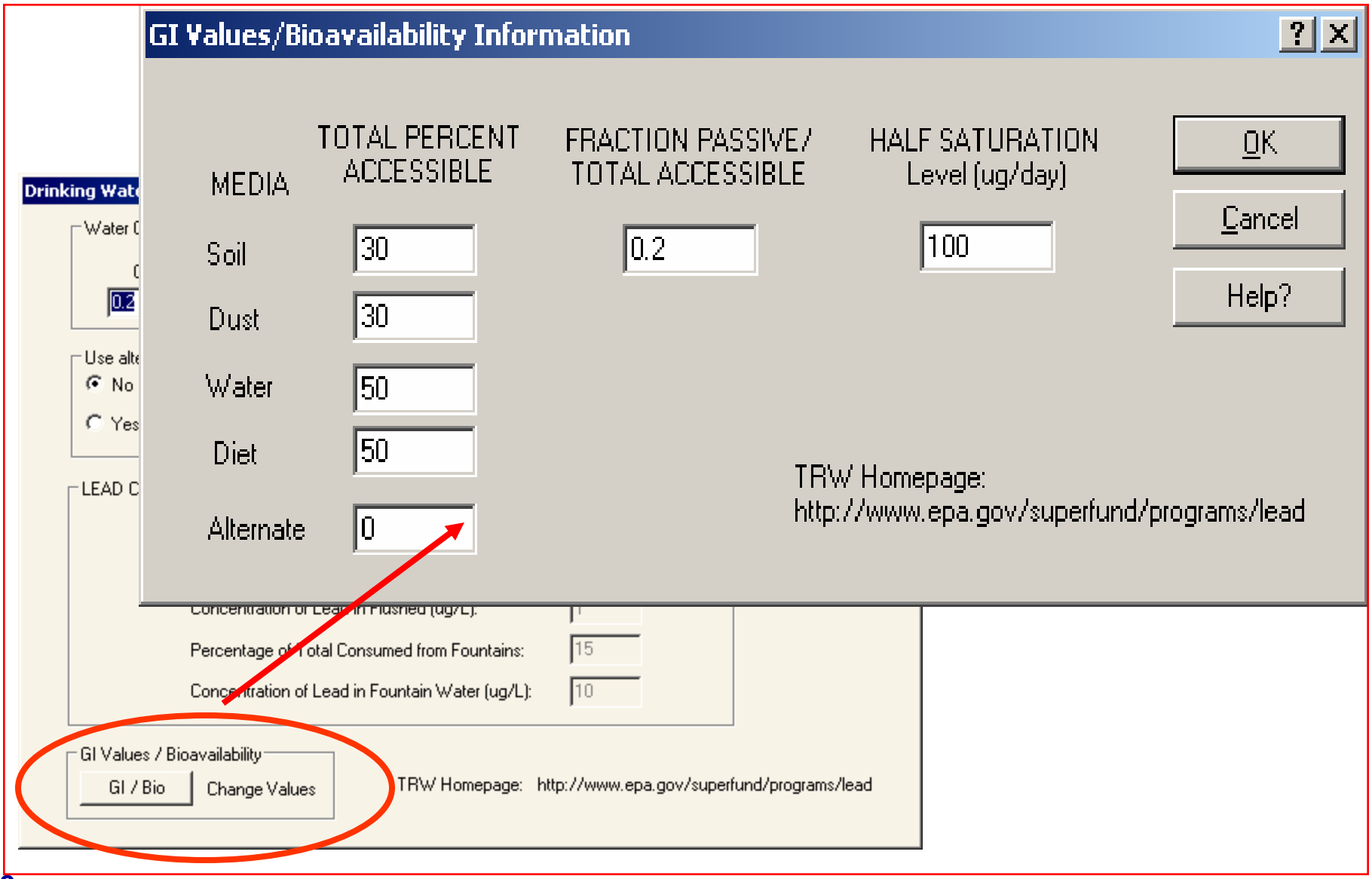
Soil and Dust Exposure Input



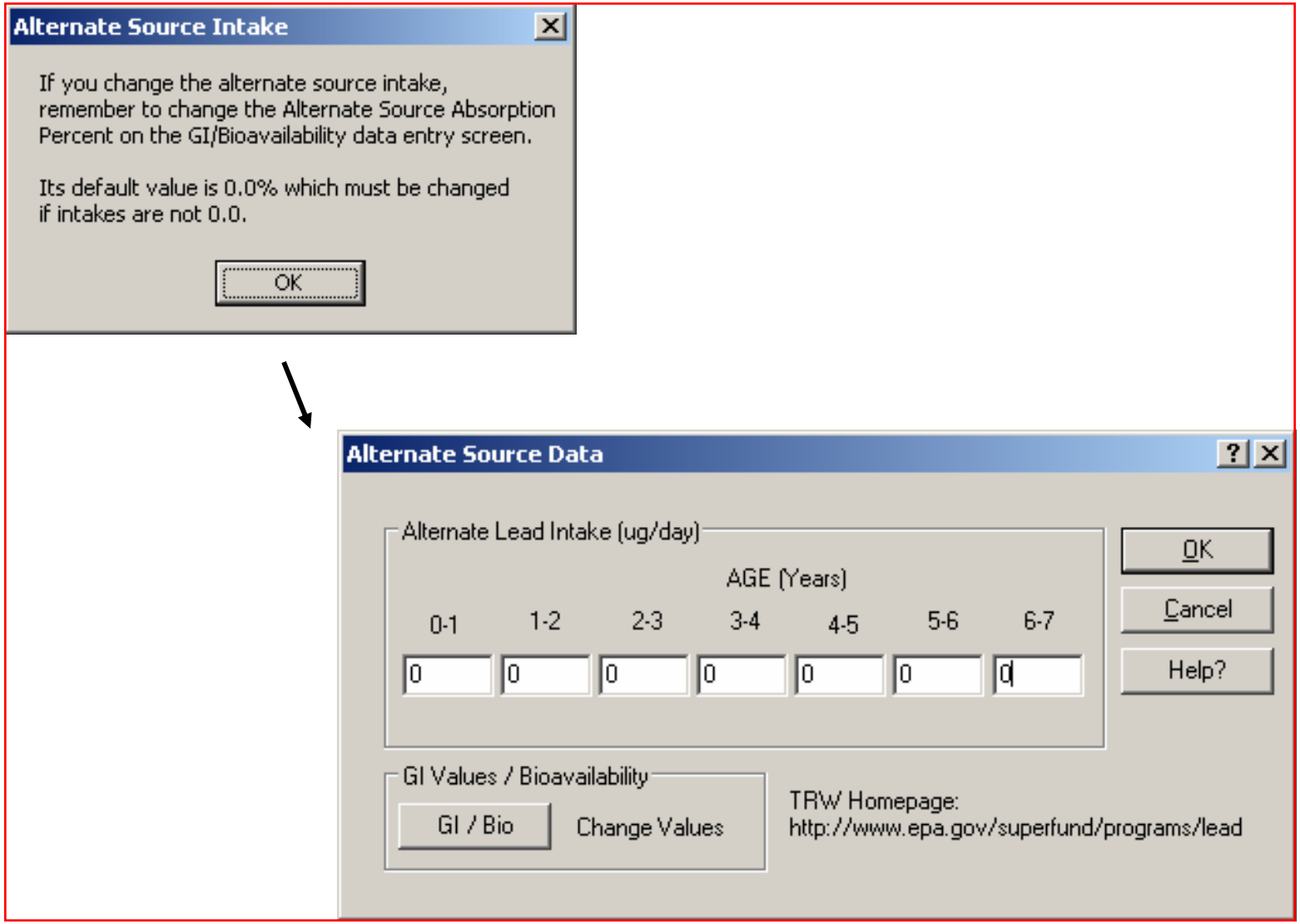
Multiple Source Analysis Detail



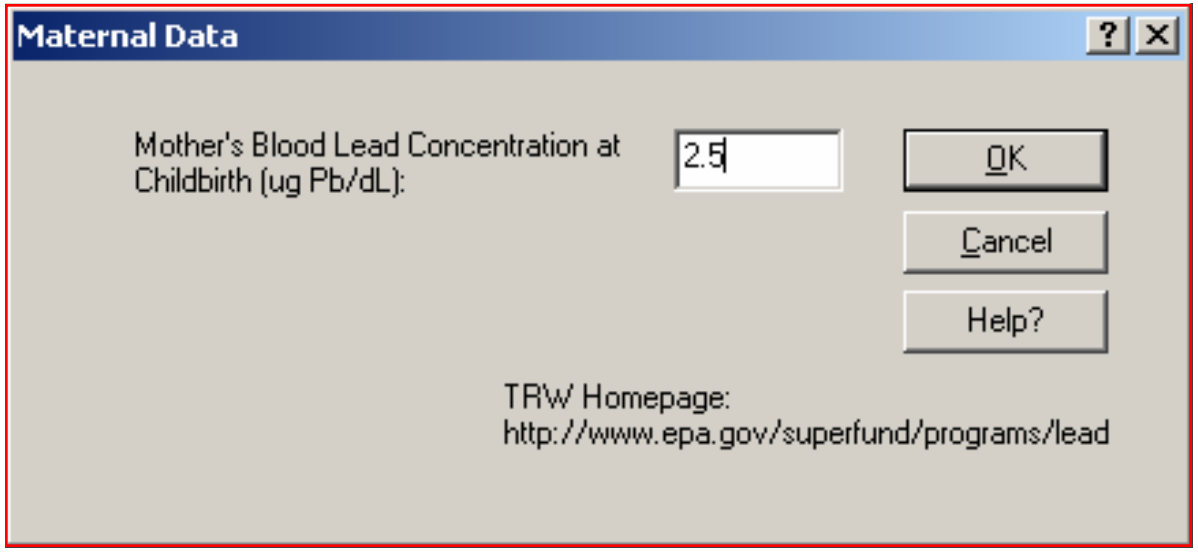
Bioavailability Information Input



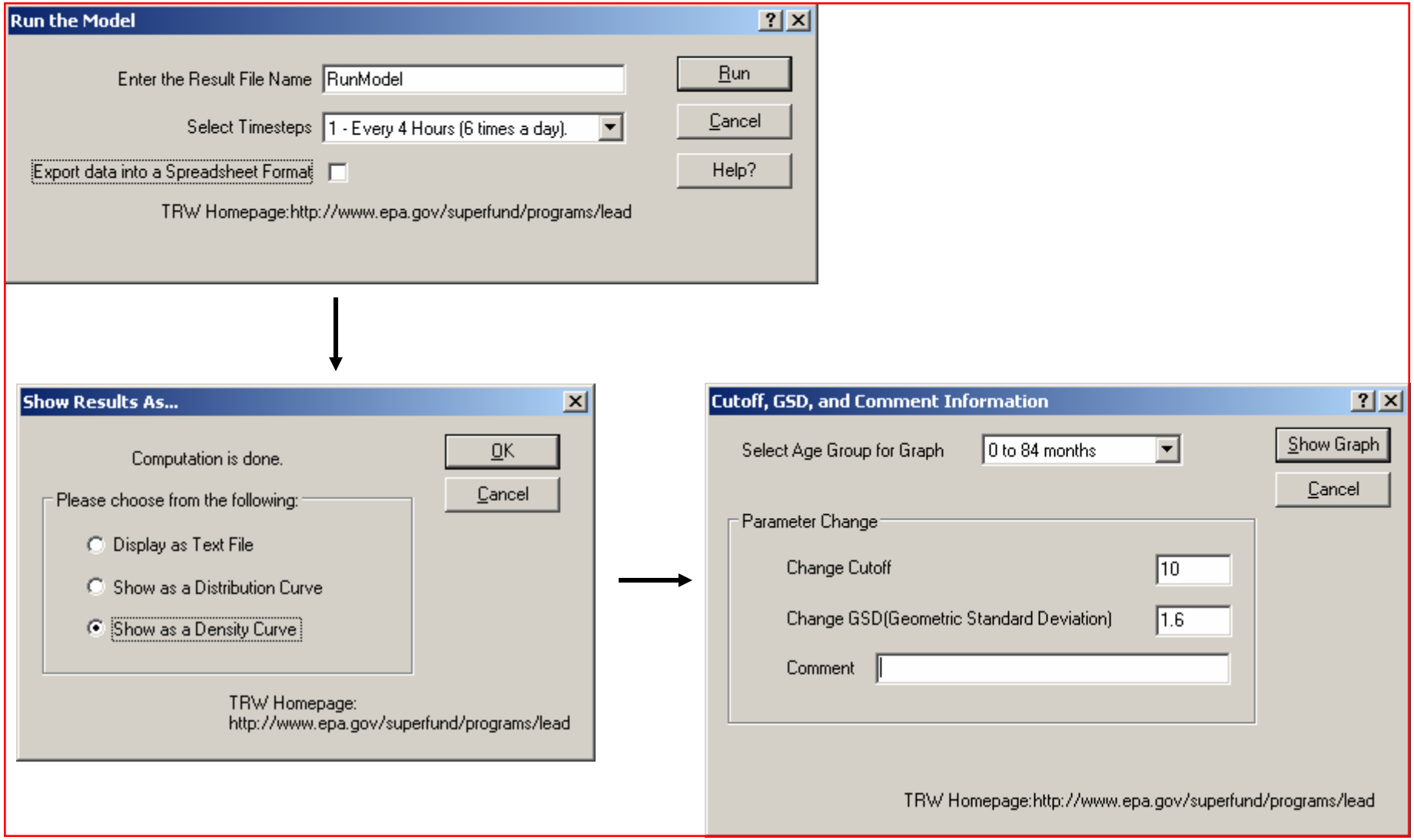
Alternate Exposure Input



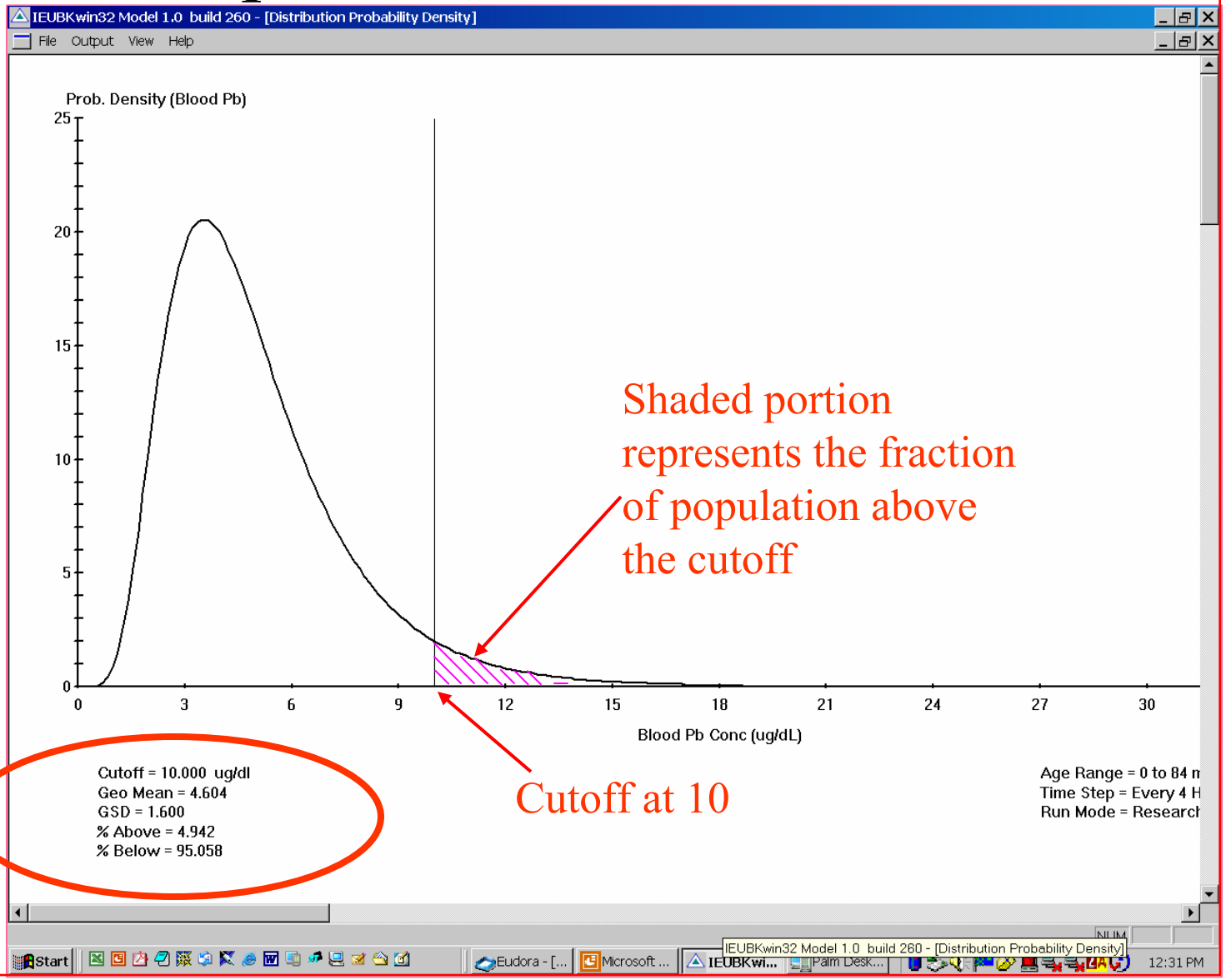
Maternal Exposure Input



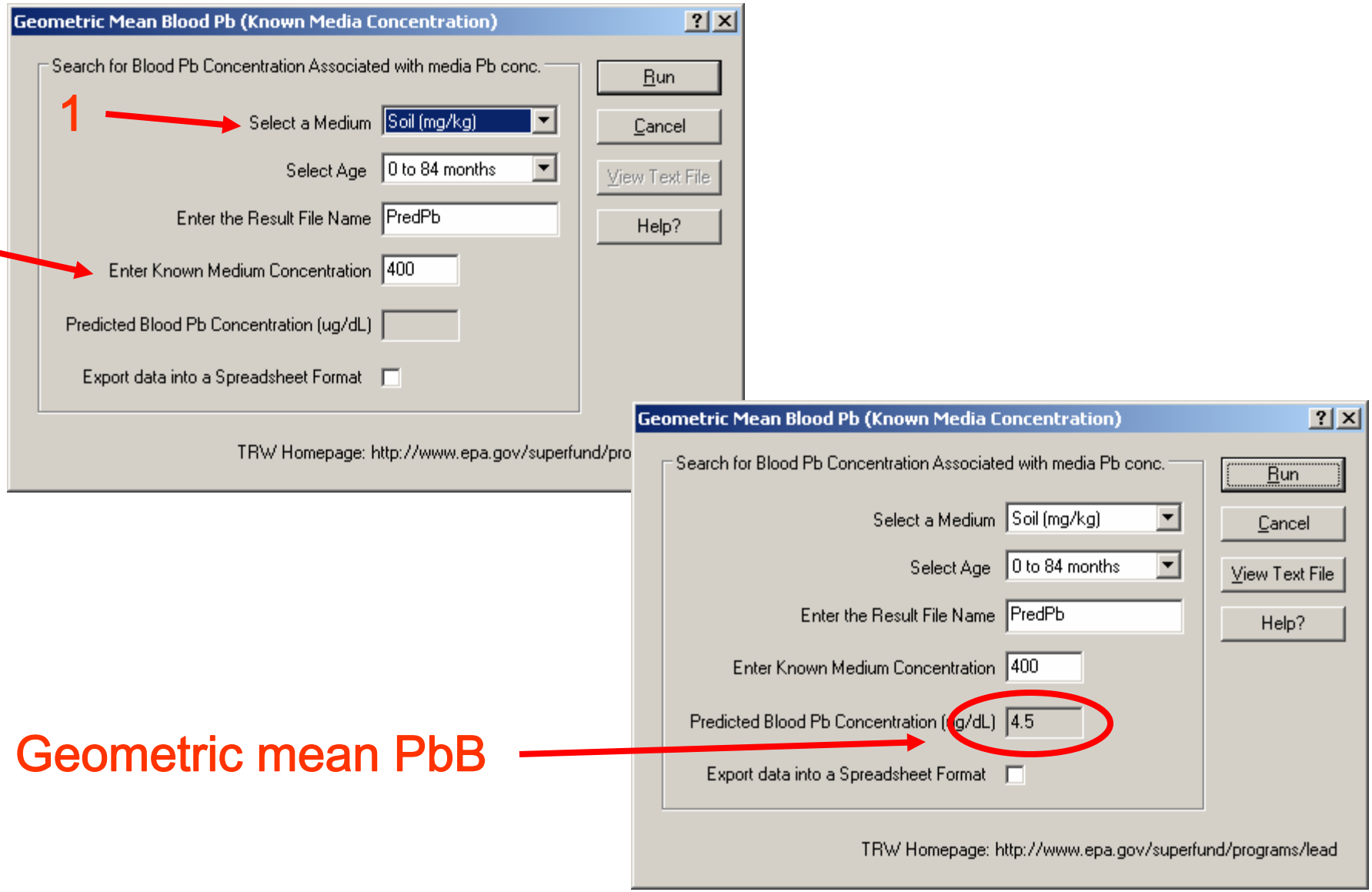
Run Risk Calculation (forward equation)



Output from the IEUBK Model



Run PRG Calculation (backward equation)



Evaluation and Validation of the IEUBK

IV&V evaluated the following:

1. Scientific underpinnings of the model structure
2. Adequacy of parameter estimates
3. Mathematical relationships (as computer code)
4. Empirical comparisons (predicted vs. observed)

The process and results of the IEUBK validation are available online (http://epa.gov/superfund/lead)

1994 Validation Strategy for the IEUBK

1998 Empirical Comparisons Manuscript (Hogan et al., 1998)

Comparison of IEUBK Predictions and Observed PbB

Comparison of Observed and Predicted Geometric Mean Blood Lead and Risk of Exceeding 10 µg/dL for Three Community Blood Lead Studies

Dataset	N	Observed Blood Lead (µg/dL)		Model Predictions (µg/dL)	
		GM (95% CI)	Percent >10 (95% CI)	GM (95% CI)	Percent >10 (95% CI)
Galena, KA Jasper Co, MI[a]	111	5.2 (4.5-5.9)	20 (13-27)	4.6 (4.0-5.3)	18 (11-25)
Madison Co, IL[a]	333	5.9 (5.5-6.4)	19 (15-23)	5.9 (5.4-6.3)	23 (19-28)
Palmerton, PA[b]	34	6.8 (5.6-8.2)	29 (14-44)	7.5 (6.6-8.6)	31 (16-47)

Excerpts from Air Criteria Document for Lead (October 2006). Original data from Hogan et al. (1998)

CI, confidence interval; GM, geometric means
[a]Children away from home ≤10 hours/week
[b]Children away from home ≤20 hours/week

Sensitivity Analysis

- Predicted PbB and total lead uptake were most sensitive to the amount of soil/dust ingested per day
- Predicted PbB and total lead uptake were moderately sensitive to the following (listed in decreasing relative sensitivity):
  - absorption fraction for soil dust and diet,
  - soil lead concentration,
  - indoor dust lead concentration,
  - dietary lead concentration,
  - contribution of soil lead to indoor dust lead, and
  - half-saturation absorbable intake (based on output-input ratio).
- The predicted probability of exceeding a specified level of concerns is very sensitive to changes in the GSD.

IEUBK Strengths and Limitations

- Strengths:
  - Risk predictions and PRG over a range of exposure scenarios
  - Inputs tailored to support Superfund site risk assessment
  - Risk information complementary to a public health study or when no public health study is available

- Limitations:
  - Cannot assess short-term, periodic or acute exposures (exposures must be for at least 1 day per week for 90 consecutive days)
  - Cannot assess pica exposures
  - Cannot assess dust exposures using loading data
  - Cannot assess age groups > 7 years

EPA Adult Methodology (ALM)

- Adopted and modified from Bowers et al. (1994)
- Uses a simplified biokinetic slope factor (BKSF)
- Slope relates change in PbB (µg/dL) per µg/day Pb absorbed
- Exposure and other variables differ from IEUBK (IR, bioavailability, etc.)

ALM Spreadsheet (Risk Calculation)

Exposure Variable	Description of Exposure Variable	Units	Region OR Ethnic GSDi and PbBo Data from NHANES III Analysis All/All
PbS	Soil lead concentration	ug/g or ppm	1197
$R_{fetal/maternal}$	Fetal/maternal PbB ratio	--	0.9
BKSF	Biokinetic Slope Factor	ug/dL per ug/day	0.4
GSD_i	Geometric standard deviation PbB	--	2.1
PbB_0	Baseline PbB	ug/dL	1.5
IR_S	Soil ingestion rate (including soil-derived indoor dust)	g/day	0.050
IR_{S+D}	Total ingestion rate of outdoor soil and indoor dust	g/day	--
W_S	Weighting factor; fraction of IR_{S+D} ingested as outdoor soil	--	--
K_{SD}	Mass fraction of soil in dust	--	--
$AF_{S,D}$	Absorption fraction (same for soil and dust)	--	0.12
$EF_{S,D}$	Exposure frequency (same for soil and dust)	days/yr	219
$AT_{S,D}$	Averaging time (same for soil and dust)	days/yr	365
PbB_{adult}	**PbB of adult worker, geometric mean**	**ug/dL**	**3.3**
$PbB_{fetal,0.95}$	95th percentile PbB among fetuses of adult workers	ug/dL	10.0
PbB_t	Target PbB level of concern (e.g., 10 ug/dL)	ug/dL	10.0
$P(PbB_{fetal} > PbB_t)$	**Probability that fetal PbB > PbB_t, assuming lognormal distribution**	**%**	**5.0%**

Recommended PbB_0 and GDS_i Input

Estimated GM PbB_0 and GSD of US Women (17-45 years)				
Subpopulation	***n***	**GM PbB (µg/dL)**	**GSD**	**PRG (ppm)**
All Census Regions Combined				
All races	5016	1.53	2.11	1197
Non-Hispanic white	1529	1.45	2.09	1288
Non-Hispanic black	1692	1.78	2.16	938
Mexican-American	1562	1.70	2.29	794
All Races/Ethnic Groups Combined				
Northeast Region	629	1.98	2.00	1092
Midwest Region	945	1.53	2.18	1079
South Region	2159	1.39	2.07	1366
West Region	1283	1.40	2.11	1287

Guidance for the IEUBK and ALM

- Model documentation (user's guides and validation information)
- Short Sheets
  - Recommendations for Sampling and Analysis of Soil at Lead Sites
  - Soil/Dust Ingestion Rate
  - Mass Fraction of Soil in Indoor Dust (MSD)
  - Intermittent or Variable Exposures at Lead Sites
- Residential Sites Handbook
- Assessing Intermittent or Variable Exposures at Lead Sites
- Bioavailability Guidance
- Frequently Asked Questions (FAQs)

http://www.epa.gov/superfund/lead

New Bioavailability Guidance

Guidance for Evaluating the Oral Bioavailability of Metals in Soils for Use in Human Health Risk Assessment

United States
Environmental
Protection Agency

OSWER 9285.7-80

Guidance for Evaluating the Oral Bioavailability of Metals in Soils for Use in Human Health Risk Assessment

---

EPA

OSWER 9285.7-77
May 2007

ESTIMATION OF RELATIVE BIOAVAILABILITY OF LEAD IN SOIL AND SOIL-LIKE MATERIALS USING *IN VIVO* AND *IN VITRO* METHODS

Case Studies

1. IEUBK: Single run with 500 ppm soil and default (old) dietary data. Risk calculation.

2. IEUBK: Single run with 500 ppm soil and new dietary data (attached). Risk calculation.

3. IEUBK: PRG calculation using new dietary data and modified drinking water value. Also saving and reloading a data file and reset all parameters.

4. IEUBK: Multiple runs for soil range using new dietary data and modified drinking water value. Plot of risk calculations.

5. IEUBK: Find media concentration for soil without and with new dietary data and interpretation of GM PbB output.

6. IEUBK: Creating a batch mode input file from a spreadsheet file (attached).

7. IEUBK: Running a batch mode to calculate risk.

8. ALM: Example data entry for non-residential scenario. Calculation of risk and PRG.

TRW Lead Committee

Co-Chairs

- Mike Beringer (Region 7)
- Jim Luey (Region 8)

Executive Secretary: Aaron Yeow (OSRTI HQ)

Superfund Lead Webpage:
www.epa.gov/superfund/lead

Contact the TRW hotline

- Send an e-mail to pbhelp@epa.gov
- Call the toll-free TRW hotline at 1-866-282-8622

Wrap up

EPA provides risk tools and guidance to assess lead exposure at hazardous waste sites. The Lead Committee of EPA's Technical Review Workgroup for Metals and Asbestos (TRW) is available to support users when questions or when novel applications arise

- Evaluate & develop models and other risk tools
- Provide technical support for the development and implementation of EPA guidance on lead
- Review application of risk assessment tools
- Provide technical assistance to end users for use of non-standard (site-specific) values

TRW Lead Committee Members are EPA staff from Regions, Headquarters, and Labs